

**REMARKS**

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

The Office Action Summary correctly indicates that claims 40-42, 44, 46, 47, 51-58 and 60 are pending in the application. All claims are directed to the elected invention. Claims 40-42, 44, 46, 47, 51-58 and 60 are under consideration and stand rejected.

By the present amendment, the sequence listing is replaced by a substitute sequence listing, which incorporates two peptide sequences that were inadvertently omitted from the original sequence listing. Amendments to the specification are made to insert SEQ ID identifiers in the text where appropriate.

Claims 51 and 58 have been amended to insert the word “and” before the last item in the Markush groups recited therein. Claim 55 has been amended to correct an error and restore superscripts that were misformatted in the claim listing of the previous Amendment.

Claims 40, 44, and 60 have been amended to replace the phrase “directed against” with “capable of recognizing,” which is supported at least at page 16, lines 28-30. Claim 44 has been further amended to more clearly describe the claimed subject matter by rearranging the clauses and punctuation thereof. Claim 44 has been further amended to be more grammatically proper.

No prohibited new matter has been introduced by way of the above amendments. Applicants reserve the right to file a continuation or divisional application on subject matter canceled by way of this Amendment.

**Rejections under 35 U.S.C. § 112**

Claims 42, 44, 57, 58 and 60 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to satisfy the written description requirement. The rejections are respectfully traversed.

**Regarding Claims 42 and 60**

With respect to claim 42, the Office has alleged that the original disclosure does not support fusion of both the extracellular domains I and II of CD4 and a generic toxic substance to a specific or generic antibody or part thereof. Claim 60 has been previously rejected on these grounds. The Office has acknowledged that the original specification discloses a species within the scope of these claims. The Office Action mailed April 23, 2004 acknowledges that support for, at least a species of the claimed invention, can be found in the original specification at pages 13, 18, and original claim 28.

Applicants respectfully submit that for the reasons presented in the Amendment and Reply filed March 8, 2004, and as further discussed below in response to remarks of the present Office Action, it would be apparent to one of skill in the art from the disclosure taken as a whole, including the Examples and the original claims, that the combinations claimed in claims 42 and 60 were considered as an embodiment of the invention by the inventors at the time the application was filed.

The specification and original claims demonstrate that Applicants considered the invention as now claimed to be included in the invention at the time the application was filed.

Applicants note that more support appears in the original disclosure than is cited in the Office Action. For example, Applicants further direct the Office's attention to Figure 11 and Example 6 for specific disclosures of preferred embodiments. More generally, the original claims make it apparent that the original claims encompassed the claimed

combinations. For example, original claim 27 recited an antibody fused to domains of CD4 (the immunopotentiating substance recited in claim 42 by dependence on claim 40). Original claim 27 depended from claim 24, which depended from claim 21, which recites that the antibody can be modified by a toxic substance chosen from a group that parallels the group recited in present claim 42. Original claim 21 depended from claim 20, which recites that the antibody, or part thereof, of claim 18 is modified by a toxic or immunopotentiating substance.

Thus, consistent with the disclosure as a whole, at least the original claims 27, 24, 21, 20 and 18 clearly evidence that Applicants considered that the invention included embodiments encompassed by claim 42 wherein the antibody, or antibody fragment, was fused to either or both of an immunopotentiating substance (such as the I and II domains of CD4 recited in claim 27) and a toxic substance (such as those recited in original claim 21).

The case law relied upon by the Office does not support the rejection.

The Office relies on the following cases in support of the rejection: *Purdue Pharma L.P. v. Faulding Inc.*, 56 USPQ2d 1481 (Fed. Cir. 2000), *In re Shokal*, 113 USPQ 283 (CCPA 1957), and *Lockwood v. American Airlines*, 41 USPQ2d 1961 (Fed. Cir. 1997).

*Purdue Pharma* is cited at page 5 of the Office Action mailed April 23, 2004. Applicants respectfully submit that the holding of insufficient written description in *Purdue Pharma* does not control this case, because the present circumstances are quite different from the circumstances under which the written description in that case was held insufficient. *Purdue Pharma* concerns the question of whether a property of a compound that is revealed only by derivation from experimental results disclosed as examples in a specification, but not otherwise remarked upon, can be the basis of a claim limitation. In the present circumstance, toxic substances and immunopotentiating substances were described as optional features of the invention throughout the specification with numerous examples of each provided.

The question in this case is different from the question presented in *Purdue Pharma*. The question here is whether it is proper to claim a combination comprising two different features that are described as optional alternative features in the specification that are also disclosed in combination in a preferred exemplary embodiment.

The Office appears to have applied an unreasonably exclusive construction of the use of “or” in the original claims. It would be simply unreasonable to construe original claims and the specification in a manner that excludes embodiments having a combination of features disclosed in a preferred embodiment that is described in detail in an example and illustrated in drawings. It is further unreasonable to construe the term “or” as an exclusive “or” where original dependant claims prove that original parent claims reciting “or” between optional alternative features included combinations of the optional alternative features.

The Federal Circuit Court has affirmed a holding that the word “or” in claims can include the combination “and” where the specification indicates that was an intended meaning. *Brown v. 3M*, 60 USPQ2d 1298 (D. Ariz. 2000), *aff'd* 60 USPQ2d 1375 (Fed. Cir. 2001) (holding that “or” can be inclusive, describing a list of alternative things in which one may choose one option or any combination of alternative options). This may be distinguished from *Kustom Signals v. Applied Concepts*, 60 USPQ2d 1135 (Fed. Cir. 2001) where “either ... or” in Kustom’s claims meant exclusive alternatives, because there was no basis whatsoever for believing that Kustom meant otherwise. The construction of “or” that that the Federal Circuit affirmed in *Brown* was consistent with ordinary usage of the term. For example, if a baseball league’s rules stated that a ballgame can be terminated due to lightning *or* hail, one would also expect a game to be canceled in the case of lightning *and* hail. Thus, it is reasonable to construe the term “or” to include both alternatives and

combinations of alternatives, and in this case it is unreasonable to hold that the applicants intended the usage of “or” as an exclusive term.

*Purdue Pharma* does set forth a test for the sufficiency of written description that is relevant. The Federal Circuit Court states:

In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide *in haec verba* support for the claimed subject matter at issue. See *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1570, 39 USPQ2d 1895, 1904 (Fed. Cir. 1996). Nonetheless, the disclosure “must . . . convey with reasonable clarity to those skilled in the art that . . . [the inventor] was in possession of the invention.” *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Put another way, one skilled in the art, reading the original disclosure, must “immediately discern the limitation at issue” in the claims. *Waldemar Link GmbH & Co. v. Osteonics Corp.*, 32 F.3d 556, 558, 31 USPQ2d 1855, 1857 (Fed. Cir. 1994). That inquiry is a factual one and must be assessed on a case-by-case basis. See *Vas-Cath*, 935 F.2d at 1561, 19 USPQ2d at 1116 (“Precisely how close the original description must come to comply with the description requirement of § 112 must be determined on a case-by-case basis.”).

*Purdue Pharma* at 1483. *Purdue Pharma* also refers to a need for “blazemarks” in a specification to indicate what the applicants considered to be features of the invention at the time the application was filed. Applicants respectfully submit that that the present specification meets the *Purdue Pharma* test in that the immunopotentiating substance and toxic substance features are described generally and through specific examples, throughout the specification and at least the working examples, drawings, and original claims provide more than adequate “blazemarks” to the combinations recited in claims 42 and 60.

*In re Shokal*, also cited at page 5 of the Official Action, does not lead to the Office’s asserted holding either. *In re Shokal* concerns the question of whether it is proper to claim a genus where the genus is not explicitly described in an application but is defined only by properties of a limited number of examples. In *Shokal*, the appellants sought to claim a polymer generically when only a limited number of species were disclosed. The appellants in *Shokal* were seeking to obtain broader generic claims that would encompass specific subject

matter that had been lost in an interference. In the present rejection, the Office appears to allege that claims 42 and 60 each encompass a genus that is insufficiently represented by the exemplary embodiments of the invention that are disclosed.

However, unlike the case in *In re Shokal*, present claims 42 and 60 do not encompass broader subject matter than was previously claimed. In claim 42, Applicants seek to obtain a claim that is dependant on claim 40 and recites additional features in combination with the features recited in claim 40. Any concern with the number of species encompassed in claims 42 and 60, and basing the rejection thereon, is logically inconsistent with the fact that the sufficiency of the written description of the genus of claim 40 as currently presented and as previously presented has been acknowledged.

At page 6, the Office relies on *Lockwood v. American Airlines Inc.*, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997) in responding to arguments presented in Applicants' Amendment and Reply filed March 8, 2004. In *Lockwood*, it was held that just because something would be obvious from the disclosure of the specification, the written description requirement was not satisfied. However, Applicants have not relied upon an argument that the combination of an antibody fused to a toxic substance and an immunopotentiating substance would be obvious from the disclosure. Rather, Applicants respectfully maintain, that it would be apparent to one of skill in the art from the Examples and the original claims that the claimed combination was considered as an embodiment of the invention by the inventors at the time the application was filed.

Contrary to the implication of the Office's rejection, one of skill in the art would not have to speculate that the combinations claimed in claims 42 and 60 were envisioned by Applicants, because the Examples illustrate and the original claims explicitly encompass the combinations claimed in claims 42 and 60.

For at least the foregoing reasons, and reasons previously presented with respect to claim 60, the subject matter of claims 42 and 60 is adequately described in the specification in accordance with 35 U.S.C. § 112, first paragraph. The cases relied upon by the Office to support the rejection do not lead to a contrary finding. Accordingly, withdrawal of the rejection is respectfully requested.

**Regarding Claims 44, 57 and 58**

Claims 44, 57 and 58 are rejected, because the specification allegedly does not describe multimeric protein comprising a heavy and a light chain, both being modified at their N-terminus by fusion to extracellular domains I and II of CD4. The rejection refers in particular to the language of claim 44, from which claims 57 and 58 depend.

Applicants respectfully submit that one skilled in the art would understand that claim 44 recites that the protein of interest, which comprises a heavy chain and a light chain of an antibody, is modified at the N-terminus by fusion to extracellular domains I and II of CD4. That is to say, it is the protein of interest that is modified by fusion as recited. Claim 44 was not intended to require that both the heavy and light chains be modified at their N-terminus by fusion to extracellular domains I and II of CD4. Without agreeing with the rejection, claim 44 has been rewritten to arrange the descriptive clauses so as to emphasize the intended meaning of the claim.

The subject matter of claim 44 is described throughout the specification. For example at page 4, line 35, to page 7, line 29, the specification discloses features of antibodies and parts of antibodies that may be used in the invention, and includes, for example, the teaching at page 5, lines 15-20 that an exogenous sequence encoding a heavy and a light chain may be used to produce such a protein of interest. Immediately following this section, at pages 7,

line 30 to page 10, line 3, the optional fusion of immunopotentiating and toxic substances to antibody proteins of interest is disclosed. In this portion of the specification, the CD4 protein is taught, for example, at page 8, lines 23-39. At page 10, lines 4-8, it is disclosed that a particularly preferred construction consists in including the nucleotide sequence encoding the toxic or immunopotentiating substance 5' or 3' of a nucleotide sequence encoding all or part of an antibody.

Thus, throughout at least these sections, the specification describes an exogenous nucleotide sequence as recited in claim 44. That other features of the vectors recited in claims 44, 57 and 58 are adequately described has not been disputed. Accordingly, withdrawal of the rejection is respectfully requested.

#### **Rejections under 35 U.S.C. § 103**

Claims 40, 41, 44, 46, 47 and 51-58 have been rejected under 35 U.S.C. § 103 as allegedly unpatentable over Alloway et al. (WO 94/19017) in view of Berkner (WO 90/01550). These grounds for rejection have been previously addressed. At page 8 of the Office Action, it is noted that this ground of rejection had been previously withdrawn. However, the rejection was reinstated, upon reinterpretation of the claim terminology. Allegedly the recitation of all or part of an antibody directed against a tumor or an epitope specific for an infectious and pathogenic organism does not distinguish the generic "part" of the antibody from Alloway. In this regard, the Office asserts that Alloway teaches that CD4 extracellular domains can be fused to the constant domain regions of an antibody. The Office proposes to interpret the claim to mean that the part of an antibody recited in claim 40 might be a part that is common to all antibodies of a given type (including the constant domain regions of taught by Alloway) and alleges that such a construct would be obvious in view of

Alloway combined with Berkner. However, the interpretation of the claim proposed by the Office is unreasonable as it would render language of the claim superfluous. Therefore, for at least this reason and the reasons previously presented, the rejection is traversed.

As the grounds for rejection have previously been addressed generally, the following comments are focused on the basis now alleged for reinstating the rejection. Claim 40, as previously presented, recited “. . . an exogenous nucleotide sequence encoding all or part of an antibody directed against a tumor or an epitope specific for an infectious and pathogenic organism . . .” The antibody or part of an antibody recited in claim 40 is described as being directed against a tumor or an epitope specific for an infectious and pathogenic organism. The constant regions of the chimeric protein described by Alloway are added to increase the half-life of the CD4 molecule. See, Alloway at page 3, line 34 to page 4, line 2. The immunoglobulin constant region parts of the chimeras that Alloway describes could not reasonably be considered directed against a tumor or an epitope specific for an infectious and pathogenic organism. Contrary to the teaching of Alloway, to be directed against an epitope reasonably means that the recited “all or part of an antibody” comprise at least portions that confer the capacity and specificity to recognize the epitopes against which the antibody is directed. Such an interpretation is consistent with the teaching of the specification, for example at page 16, lines 24-31, where preferred levels of therapeutic expression of functional antibodies are disclosed and functional antibodies are defined as capable of recognizing the antigen against which it is directed.

Without agreeing with the Office's rejection, claims 40, 44, and 60 have been amended to replace the phrase “directed against” with “capable of recognizing.” For example, claim 40 now recites “all or part of an antibody capable of recognizing a tumor antigen or an epitope specific for an infectious and pathogenic organism.” That is to say, the

recited antibody or part of an antibody must be capable of recognizing the target. It would be unreasonable to construe claims 40, 44, and 60 as referring to part of an antibody that is not capable of recognizing one of the recited targets. Such a construction would render this claim language superfluous.

The antibody parts in the CD4 chimeras taught by Alloway are not directed against or capable of recognizing a tumor antigen or an epitope specific for an infectious and pathogenic organism. Berkner fails to cure the deficiencies of Alloway. Thus, for the foregoing reasons, in addition to the reasons previously presented regarding these grounds for rejection, claims 40, 41, 44, 46, 47 and 51-58 are distinguished from what is described in Alloway and Berkner. The combination of Alloway and Berkner fails to teach every element of the claimed invention and further provides no motivation to combine the references and to modify the teachings thereof in a manner that would lead one to the claimed invention. As a result, Alloway and Berkner fail to support a prima facie case of obviousness. *See*, MPEP § 2143. Accordingly, it is respectfully requested that the rejection be withdrawn again.

**CONCLUSION**

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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